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ORAL VALGANCICLOVIR IS SAFE AND EFFECTIVE AS PREEMPTIVE THERAPY FOR CMV INFECTION IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Despite significant advances in prevention and therapy CMV infection continues to be an important cause of morbidity and mortality in the hematopoietic stem cell transplant (HSCT) recipient. The standard drug for preemptive therapy of CMV is intravenous ganciclovir (GCV). Valganciclovir (VGC), the oral prodrug of GCV has excellent bioavailability and is ideal for oral therapy. Since March/2002, VGC was adopted in our center for outpatient preemptive therapy in all allogeneic HSCT recipients who develop a positive assay for CMV based on Digene® Hybrid Capture performed as weekly surveillance. **Material and methods:** A retrospective review of all patients who received Valganciclovir as preemptive therapy for CMV infection between March 1/2002 and May 31/2003 was performed. All patients had at least 100 days of post-transplant follow up. Patients with a positive CMV assay were treated with VGC 900 mg PO BID × 14 days followed by 900 mg PO QD × 7 days. **Results:** 52 allogeneic HSCT recipients were followed weekly via Digene hybrid capture assay. 18 patients (14 Allo, 4 MUD) had 30 episodes of CMV DNA detection (10 patients had 1 episode, 6 patients had 2 episodes and 2 patients had 3 or more). The rate of response (conversion from positive to negative in the next 2 weeks after VGC was started) was 93% (28/30). Two patients failed oral VGC. The first one with a severe mucositis became negative with IV GCV. The second one subsequently failed GCV and became negative in Foscarnet. During the period of the study one case of CMV enteritis was diagnosed in a patient with acute GVHD. This patient recovered with GCV. In 2 patients treatment was changed to GCV after one week due to nausea and vomiting in the setting of acute GVHD. Median duration of therapy was 21 days (range 10 to 21 days). 66% (20/30) episodes were associated with acute or chronic GVHD. The mean WBC the day VGC started was 6.5×10^9/L (range 1.9-14.5) and decreased to 3.1×10^9/L (range 0.5-13.9) at the end of the treatment. Minor changes were noticed in Hb and platelet count. Creatinine remained stable in all patients. **Conclusion:** Preemptive therapy of CMV infection with oral VGC is safe and effective in allogeneic HSCT recipients.

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PALIFERMIN REDUCES SEVERE ORAL MUCOSITIS (OM), IMPROVES PATIENT QUALITY OF LIFE, AND REDUCES HEALTH RESOURCE USE IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES RECEIVING HIGH-DOSE CHEMOTHERAPY (HDCT) AND TOTAL BODY IRRADIATION (TBI) WITH AUTOLOGOUS PERIPHERAL BLOOD STEM CELL (PBSC) SUPPORT: RESULTS FROM A PHASE III TRIAL

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Palifermin (recombinant human keratinocyte growth factor) can protect and heal the epithelial tissues lining the mouth and gut from damage caused by anticancer therapy. In animal models, palifermin reduces chemotherapy and/or radiation-induced injury to the mucosal lining of the oral cavity and lower gastrointestinal tract. Patients with hematologic malignancies undergoing HDCT and/or TBI with PBSC support frequently experience severe OM. OM has been reported by transplant recipients as the most debilitating side effect of their treatment (Bellm et al, Support Care Cancer, 2000). OM and its clinical sequelae are also associated with significant economic burden (Sonis et al, JCO, 2001). A phase 3 double-blinded study of palifermin was conducted in 212 patients with hematologic malignancies undergoing TBI (12 Gy) and HDCT (60 mg/kg etoposide and 100 mg/kg cyclophosphamide) with autologous PBSC. Patients were randomized (1:1) to placebo or palifermin 60 μg/kg/day for 3 consecutive days before TBI and 3 consecutive days after PBSC transplant. Measures of OM and patient-related outcomes (PRO), including mouth and throat soreness (MTS), were assessed daily until OM grades returned to WHO grade ≤2. PRO was assessed with a mucositis-specific daily diary and the Functional Assessment of Cancer Therapy-General (FACT-G). Palifermin reduced the incidence and duration of WHO grades 3, 4 OM and reduced clinical sequelae (Table 1); opioid analgesic use (median mg morphine equivalent palifermin 212 mg vs placebo 535 mg), and total parenteral nutrition incidence (palifermin 11% vs placebo 40%). Adverse events occurring more frequently in palifermin patients included mild skin and oral erythema with/without edema, and asymptomatic, transient increases in serum amylase and lipase. Clinical effects were accompanied by statistically significant, clinically meaningful improvements in measures of PRO, including MTS and functional and physical well-being domains of the FACT-G. Palifermin produced a >40% reduction vs placebo in patient-reported limitations related to eating*, talking*, sleeping*, swallowing*, and drinking* (*$p < 0.001$), and produced significant reductions in measures of resource utilization. We conclude that palifermin reduces the incidence and duration of severe OM in patients undergoing autologous PBSC transplant after TBI and chemotherapy conditioning, resulting in improved patient quality of life and reduced resource utilization.

Table.

	Placebo (n = 106)	Palifermin (n = 106)	*P* Value
Clinical Results:			
% patients with WHO grade 3, 4 OM	98	63	0.001<
% patients with WHO grade 4 OM	62	20	0.001<
Mean (SD) days WHO grade 3, 4 OM	10.4 (6.2)	3.7 (4.1)	0.001<
Patient-related Outcomes:*			
FACT-G functional well-being	12.7 (4.84)	14.4 (4.71)	0.03
FACT-G physical well-being	17.0 (4.13)	18.8 (4.34)	0.009
MTS	1.3 (0.53)	0.7 (0.49)	0.0001
Medical Resource Utilization:			
Mean days inpatient hospitalization†	17.3 (5.38)	15.3 (5.06)	0.008
Mean days analgesic opioid use	11.8 (5.7)	6.8 (5.7)	0.0001
Patients with parenteral feeding (%)‡	43	11	0.001<

*Mean daily area under the curve score (SD).

†For hospitalizations post-transplant, only patients with inpatient admissions were included in the analysis (99 placebo and 100 palifermin patients).

‡Due to oral mucositis.